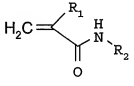
AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application. Deletion of subject matter from the claims and cancellation of claims are effected without prejudice.

LISTING OF CLAIMS:

1. (Currently Amended) A pharmaceutical composition having an anti-tumor effect comprising a pharmaceutically acceptable carrier or excipient and, as active ingredient,

- a synergistic effective amount of a compound of formula (I):

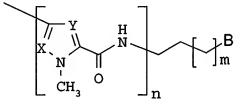


(I)

wherein:

R_1 is a bromine or chlorine atom;

R_2 is a group of formula (II)



(II)

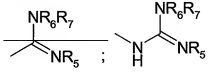
wherein

m is 0 or 1;

n is 3 or 4;

X and Y are, the same or different and independently for each heterocyclic ring, a nitrogen atom or a CH group;

B is selected from the group consisting of



$$=CONR_5R_6, \text{ [[or]]} =NHCONR_5R_6$$

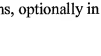
wherein R_5, R_6 and R_7, are hydrogen or a pharmaceutically acceptable salt thereof and

a protein kinase inhibitor; wherein said pharmaceutical composition has an antitumoral effect; and wherein said protein kinase inhibitor is selected from the group consisting of STI571(Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-) and OSI-774(4-Quinazolinamine, N-(3-ethynylphenyl)-6, 7-bis(2-methoxyethoxy; and the tumor to which the pharmaceutical composition has an anti-tumor effect is breast, lung, ovary, [[lung,]] colon, kidney, stomach, pancreas, liver, melanoma, leukemia and brain tumor where the antitumoral effect of said pharmaceutical composition is enhanced relative to the additive ~~antitumoral~~ anti-tumor effect of the acryloyl distamycin derivative and the protein kinase inhibitor.

2.-4. (Cancelled)

5. (Currently Amended) The pharmaceutical composition according to claim 1 comprising ~~an acryloyl distamycin derivative~~ the compound of formula (I) wherein R_1 and R_2 are as defined in claim 1, ~~r is 0,~~ m is 0 or 1, n is 4, and X and Y are both CH groups.

6. (Currently Amended) The pharmaceutical composition according to claim 5 comprising ~~an acryloyl distamycin derivative~~ the compound of formula (I) wherein R_1 is bromine, R_2 is a group of formula (II) wherein m is 0, n is 4, X and Y are CH, B is a group of formula



wherein R_5, R_6 and R_7 are hydrogen atoms, optionally in the form of a pharmaceutically acceptable salt.

7. (Currently Amended) The pharmaceutical composition ~~according to claim 1~~ comprising ~~an acryloyl distamycin derivative~~ the compound, optionally in the form of a pharmaceutically acceptable salt, selected from the group consisting of:

N-(5-{[(5-{[(5-{[(2-{[amino(imino)methyl]amino}ethyl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)-4-[(2-bromoacryloyl)amino]-1-methyl-1H-pyrrole-2-carboxamide hydrochloride;

N-(5-{[(5-{[(5-{[(2-{[amino(imino)methyl]amino}propyl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)-4-[(2-bromoacryloyl)amino]-1-methyl-1H-pyrrole-2-carboxamide hydrochloride;

N-(5-{[(5-{[(5-{[(3-amino-3-iminopropyl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)-4-[(2-bromoacryloyl)amino]-1-methyl-1H-pyrrole-2-carboxamide hydrochloride;

N-(5-{[(5-{[(5-{[(3-amino-3-iminopropyl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)-4-[(2-bromoacryloyl)amino]-1-methyl-1H-imidazole-2-carboxamide hydrochloride;

N-(5-{[(5-{[(5-{[(3-amino-3-iminopropyl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)-3-[(2-bromoacryloyl)amino]-1-methyl-1H-pyrazole-5-carboxamide hydrochloride;

N-(5-{[(5-{[(5-{[(3-amino-3-oxopropyl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)-3-[(2-bromoacryloyl)amino]-1-methyl-1H-pyrazole-5-carboxamide;

N-(5-{[(5-{[(5-{[(2-{[amino(imino)methyl]amino}ethyl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)-4-[(2-chloroacryloyl)amino]-1-methyl-1H-pyrrole-2-carboxamide hydrochloride;

N-(5-{[(5-{[(3-{[amino(imino)methyl]amino}propyl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)-4-[(2-bromoacryloyl)amino]-1-methyl-1H-pyrrole-2-carboxamide hydrochloride;

N-(5-{[(5-{[(3-amino-3-iminopropyl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)-4-[(2-bromoacryloyl)amino]-1-methyl-1H-pyrrole-2-carboxamide hydrochloride; and

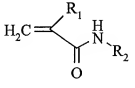
N-{5-[({5-[({5-[({3-[(aminocarbonyl)amino]propyl}amino)carbonyl]-1-methyl-1H-pyrrol-3-yl}amino)carbonyl]-1-methyl-1H-pyrrol-3-yl}amino)carbonyl]-1-methyl-1H-pyrrol-3-yl}-4-[(2-bromoacryloyl)amino]-1-methyl-1H-pyrrole-2-carboxamide.

8. (Previously Presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier or excipient and, as active ingredient,

- N-(5-{[(5-{[(5-{[(2-{[amino(imino)methyl]amino}ethyl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)-4-[(2-bromoacryloyl)amino]-1-methyl-1H-pyrrole-2-carboxamide hydrochloride (Brostallicin); and

- a protein kinase inhibitor selected from the group consisting of STI571(Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-), and OSI-774(4-Quinazolinamine, N-(3-ethynylphenyl)-6, 7-bis(2-methoxyethoxy)-),; wherein the pharmaceutical composition has an antitumoral effect which is enhanced relative to the additive antitumoral effect of the Brostallicin and the protein kinase inhibitor.

9. (Currently Amended) A product comprising a compound of formula (I):

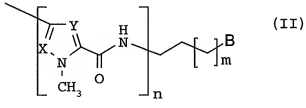


(I)

wherein:

R_1 is a bromine or chlorine atom;

R_2 is a group of formula (II)



(II)

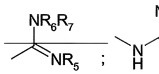
wherein

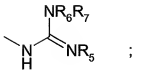
m is 0 or 1;

n is 3 or 4;

X and Y ~~are, the same or different and independently for each heterocyclic ring, a nitrogen atom or~~ a CH group;

B is selected from the group consisting of



; 

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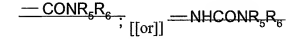

wherein R_5, R_6 and R_7, the same or different, are hydrogen;

or a pharmaceutically acceptable salt thereof; and

a protein kinase inhibitor, as a preparation where the acryloyl distamycin derivative may be administered simultaneously with the protein kinase inhibitor or, alternatively, both compounds may be administered sequentially in either order in the treatment of tumors; and wherein said protein kinase inhibitor is selected from the group consisting of STI571(Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-) and OSI-774(4-Quinazolinamine, N-(3-ethynylphenyl)-6, 7-bis(2-methoxyethoxy; wherein the product has an antitumoral effect on breast, ovary, lung, colon, kidney, stomach, pancreas, liver, melanoma, leukemia and brain tumor, which effect is enhanced relative to the additive antitumoral effect of the acryloyl distamycin derivative and the protein kinase inhibitor.

10.-12. (Cancelled)

13. (Currently Amended) The product according to claim 9 comprising ~~an acryloyl distamycin derivative~~ the compound of formula (I) wherein R_1 is bromine, R_2 is a group of formula (II) wherein m is 0, n is 4, X and Y are CH, B is a group of formula

wherein R_5, R_6 and R_7 are hydrogen, optionally in the form of a pharmaceutically acceptable salt.

14. (Currently Amended) The product according to claim 9 wherein the ~~acryloyl distamycin derivative~~ compound is selected from the group as defined in claim 7.

15. (Currently Amended) A product comprising the ~~acryloyl distamycin derivative~~ compound selected from N-[5-[[[5-[[[2-[(aminoiminomethyl)amino]ethyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-4-[[[4-[(2-bromo-1-oxo-2-propenyl)amino]-1-methyl-1H-pyrrol-2-yl[carbonyl]amino]-1-methyl-1H-pyrrole-2-carboxamide hydrochloride (Brostallicin), and a protein kinase inhibitor selected from the group consisting of STI571(Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-), OSI-774(4-Quinazolinamine, N-(3-ethynylphenyl)-6, 7-bis(2-methoxyethoxy)-) and SU 5416(2H-indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1, 3-dihydro-); as a combined preparation for simultaneous, separate or sequential use in the treatment of tumors, wherein said tumors are breast, ovary, lung, colon, kidney, stomach, pancreas, liver, melanoma, leukemia and brain tumors.

16.-23. (Cancelled)

24. (Currently Amended) A method of treating a tumor selected from breast, ~~ovary,~~ lung, ~~colon, kidney, stomach, pancreas or liver, cancer, melanoma,~~ and leukemia ~~and brain tumor~~ in a mammal, which method comprises administering to said mammal the acryloyl distamycin derivative of formula (I), as defined in claim 1, a and a protein kinase inhibitor selected from ST I571 and OSI-774, in amounts effective to produce an antitumoral effect which is enhanced relative to the additive antitumoral effect of the acryloyl distamycin derivative and the protein kinase inhibitor.

25. (Previously Presented) The method according to claim 24 wherein the acryloyl distamycin derivative is N-[5-[[[5-[[[2-[(aminoiminomethyl)amino]ethyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-4-[[[4-[(2-bromo-1-oxo-2-propenyl)amino]-1-methyl-1H-pyrrol-2-yl[carbonyl]amino]-1-methyl-1H-pyrrole-2-carboxamide hydrochloride (Brostallicin), and the protein kinase inhibitor is selected from the group consisting of STI571(Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-), OSI-774(4-Quinazolinamine, N-(3-ethynylphenyl)-6,

7-bis(2-methoxyethoxy)-) and SU 5416(2H-indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1, 3-dihydro-).

26. (Currently Amended) The method for lowering the side effects caused by antineoplastic therapy with an antineoplastic agent, in a mammal in need thereof, the method comprising administering to said mammal a combined preparation comprising a protein kinase inhibitor and a compound of formula (I), as defined in claim 1, in amounts effective to produce an antitumoral effect on tumors selected from breast, ~~ovary,~~ lung~~, colon, kidney, stomach, pancreas, liver, melanoma,~~ and leukemia ~~and brain tumors~~ which is enhanced relative to the additive antitumoral effect of the acryloyl distamycin derivative and the protein kinase inhibitor.

27. (Previously Presented) The method according to claim 26 wherein the compound of formula I is N-[5-[[[5-[[[2-[(aminoiminomethyl)amino]ethyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-4-[[[4-[(2-bromo-1-oxo-2-propenyl)amino]-1-methyl-1H-pyrrol-2-yl[carbonyl]amino]-1-methyl-1H-pyrrole-2-carboxamide hydrochloride (Brostallicin), and the protein kinase inhibitor is selected from the group consisting of STI571(Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-), OSI-774(4-Quinazolinamine, N-(3-ethynylphenyl)-6, 7-bis(2-methoxyethoxy)-) and SU 5416(2H-indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1, 3-dihydro-).

28.-30. (Cancelled)

31. (Previously Presented) The method of treating a mammal according to Claim 24 wherein the mammal is human.

32. (Previously Presented) The method for lowering the side effects according to Claim 26 wherein the mammal is human.

33.-34. (Cancelled)